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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,671	07/02/2003	Tod R. Smeal	034536-0407	5378

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EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,671	SMEAL ET AL.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-103* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 2, 7, 9, 52-55 and 64-72 are drawn to an isolated nucleic acid encoding a polypeptide or a peptide, a vector, and a host comprising same, classified in class 536, subclass 23.1, and class 435, subclass 69.1, for example.

II. Claim 3-6, 8, 10-12, 39-46, 73-89 and 94 are drawn to an isolated GEF-H1b polypeptide or peptide, a GEF-H1/PAK4 complex, a recombinant polypeptide that binds to a GEF or with homology to PAK4 fragment, and a pharmaceutical composition thereof, classified in class 530, subclass 350 and subclass 300, for example.

III. Claims 21-26 are drawn to a GEF-H1 specific antibody, classified in class 530, subclass 387.1, for example.

IV. Claims 13-18 and 20 are drawn to a method for detecting PAK4 activity in a sample, comprising detecting phosphorylated GEF-H1, classified in class 435, subclass 375, for example.

V. Claims 19, 27-34, 36-38 and 95-101 are drawn to a method of identifying a substance that modulates the interaction between PAK4 and GEF-H1 polypeptide or that inhibits PAK4 kinase activity, a method for determining whether a candidate substance inhibits PAK4 kinase activity in a mammal, a method for determining the presence of activated PAK4 in a cell sample,

or a method of inhibiting PAK4-mediated phosphorylation of a guanine nucleotide exchange factor, classified in class 435, subclass 7.1 and subclass 375,class 514, subclass 2, for example.

VI. Claim 35 and 56-60 is drawn to a method for treating cancer, comprising administering a substance, or inhibiting GEF-H1 activity in an individual, classified depending on the structure of the substance.

VII. Claims 47-51 are drawn to a method for detecting cell proliferation, cell mobility and/or cell invasion in a mammal, comprising monitoring the phosphorylation levels of GEF-H1 at different time points, classified in class 435, subclass 375, for example.

VIII. Claims 61-63 are drawn to a method for reducing cell proliferation and anchorage-independent cell growth, comprising inhibiting GEF-H1 activity in a cell sample, classified in class 435, subclass 375, for example.

IX. Claims 90-93 are drawn to a method for detecting the presence of a guanine nucleotide exchange factor in a sample comprising determining the presence of a GEF/PAK4 complex, classified in class 435, subclass 375, for example.

X. Claims 102 is drawn to a method for identifying a molecule that disrupts an interaction between PAK4 and a GEF, comprising detecting dissociation of the GEF and a polypeptide, classified in class 435, subclass 375, for example.

XI. Claim 103 is drawn to a method of inhibiting PAK4 phosphorylation of a GEF-H1, comprising introducing a polynucleotide into a cell, classified in class 435, subclass 455, for example.

The inventions are distinct, each from each other because of the following reasons:

Inventions I-III are drawn to patentably distinct products, wherein each has a different structure and function which require separate searches, and wherein each is capable of separate manufacture and use.

The polypeptides of Invention II are related to the polynucleotides of Invention I by virtue of encoding the same. Although the DNA molecules and proteins are related since the DNA encodes the specifically claimed protein, they are distinct inventions because they are physically and functionally distinct chemical entities. Further, the protein product can be made by another and materially different process, such as by purification from the natural source, and the DNA may be used for processes other than the production of the protein, such as nucleic acid hybridization assay.

The polypeptide of Invention II is related to the antibody of Invention III by virtue of being the cognate antigen, necessary for the production of the antibodies. Although the protein and antibody are related due to the necessary stearic complementarity of the two, they are distinct inventions because they are physically and functionally distinct chemical entities. For instance, the polypeptide of Invention II is a single chain that functions as an enzyme, whereas the antibodies of Invention III including IgG comprises 2 heavy and 2 light chains containing constant and variable regions, including framework regions which act as a scaffold for the 6 complementary determining regions

(CDRs) that function to bind an epitope. Thus, the polypeptide of Invention II and the antibody of Invention III are structurally distinct molecule. Further, the polypeptide of Invention II is a large molecule which contains potentially hundreds of regions to which an antibody must bind, whereas the antibody of Invention III is defined in terms of its binding specificity to a small structure within the disclosed SEQ ID NO. Thus, immunization with the polypeptide of Invention II would result in the production of antibodies outside the scope of Invention III. Therefore, the polypeptide and antibody are patentably distinct.

The antibody of Invention III is distinct from and unrelated to the polynucleotide of Invention I because they are physically and functionally distinct chemical entities which share neither structure nor function. Also, neither is required for the manufacture of the other.

Invention I and Inventions IV-X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the product of Invention I are not used or otherwise involved in the process of Inventions IV-X.

Invention I and Invention XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as

claimed can be used in a materially different method. For instance, the nucleic acid of Invention I can be used for hybridizations.

Inventions II and each of Inventions IV-X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in a materially different method. For instance, the polypeptide or peptide of Invention II can be used for making antibodies.

Invention II and Inventions XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the product of Invention II are not used or otherwise involved in the process of Inventions XI.

Inventions III and each of Inventions IV, V, VII, IX and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in a materially different method. For instance, the antibody of Invention III can be used for protein purification.

Invention III and Inventions VI, VIII and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the product of Invention III are not used or otherwise involved in the process of Inventions VI, VIII and VI.

Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: Inventions IV-XI are directed to methods that are distinct both physically and functionally, and are not required one for the other. Invention IV requires search and consideration of detecting PAK4 activity in a sample comprising detecting phosphorylated GEF-H1, which is not required by others. Invention V requires search and consideration of identifying a substance or screening drug, which is not required by others. Invention VI requires search and consideration of treating cancer, which is not required by others. Invention VII requires search and consideration of detecting cell proliferation, cell mobility and/or cell invasion in a mammal, which is not required by others. Invention VIII requires search and consideration of reducing cell proliferation and anchorage-independent cell growth comprising inhibiting GEF-H1 activity in a cell sample, which is not required by others. Invention IX requires search and consideration of detecting the presence of a guanine nucleotide exchange factor in a sample comprising determining the presence of a GEF/PAK4 complex, which is not required by others. Invention X requires search and

consideration of identifying a molecule that disrupts an interaction between PAK4 and a GEF comprising detecting dissociation of the GEF and a polypeptide, which is not required by others. Invention XI requires search and consideration of inhibiting PAK4 phosphorylation of a GEF-H comprising introducing a polynucleotide into a cell, which is not required by others. Therefore, a search and examination of both methods in one patent application would result in an undue burden, since the searches for the both methods are not co-extensive and the subject matter is divergent.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, separate search requirements, and/or different classification, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention:

A. A peptide:

A-a. SEQ ID NO: 3

A-b. SEQ ID NO: 4

A-c. SEQ ID NO: 6

A-d. SEQ ID NO: 20

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, no claim is generic.

One species from the peptide group must be chosen to be fully responsive.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

This application contains claims directed to the following patentably distinct species of the claimed invention:

B. A polypeptide:

B-a. SEQ ID NO: 2

B-b. SEQ ID NO: 21

B-c. SEQ ID NO: 22

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, no claim is generic.

One species from the polypeptide group must be chosen to be fully responsive.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain

dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D. whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
June 22, 2006

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER